reported response to therapy of the syndromes in many organ systems. Some of the syndromes, such as neurologic dysfunction, have been documented to resolve in only a small number of patients and may be explained by the relatively ineffective therapy for the neoplasm, irreversible damage to cells, tissues and organs (such as the central nervous system) or an independent or unrelated cause and pathogenesis for the syndrome.

Documented reduction or resolution of paraneoplastic effects has followed resection of several types of neoplasms. Unfortunately, many paraneoplastic syndromes are more often recognized with advanced metastatic neoplasms, many of which are currently ineffectively treated. As therapy improves, particularly for metastatic neoplasms, we are likely to observe alleviation in many of the associated syndromes after administration of effective antineoplastic therapy. In the past 15 years, curative chemotherapy has been developed for a portion of patients with several metastatic neoplasms: acute lymphocytic leukemia, choriocarcinoma, Hodgkin's disease, diffuse high-grade non-Hodgkin's lymphoma, testicular carcinoma and other germ cell neoplasms, ovarian carcinoma, acute myelogenous leukemia, Wilms' tumor, embryonal rhabdomyosarcoma, Ewing's sarcoma and small cell lung cancer. In addition, patients with several other advanced cancers—breast carcinoma, low-grade indolent non-Hodgkin's lymphoma, chronic leukemia and many others—respond favorably to chemotherapy and, although not cured, enjoy an improved survival. The paraneoplastic syndromes associated with these neoplasms are likely to improve or resolve with antineoplastic therapy, but this clinical question has not usually received emphasis in most reports. There are several well-known and accepted examples, however, of remarkable reduction in paraneoplastic phenomena with effective combination chemotherapy. The "B symptoms" (fever, weight loss, night sweats) and pruritus with Hodgkin's disease and non-Hodgkin's lymphoma regularly resolve following chemotherapy and remission of the tumor. The majority of patients with Hodgkin's disease and diffuse high-grade non-Hodgkin's lymphoma are now cured. Gynecomastia is seen in some men with germ cell tumors, particularly those with choriocarcinoma elements and elevated plasma human chorionic gonadotropin levels. The hormone level drops and gynecomastia usually resolves after effective combination chemotherapy for the germ cell tumor. Most of these patients are also cured. The hyponatremia of the syndrome of inappropriate antidiuretic hormone secretion seen in approximately 10% of patients with small cell lung cancer at diagnosis usually resolves within three to six weeks after combination chemotherapy, but often recurs with tumor relapse. A few of these patients are also cured of their neoplasm. Before effective antineoplastic therapy was developed, these groups of patients continued to suffer from the neoplastic growth and the paraneoplastic effects. In the future, with newer and more effective approaches to the therapy for many neoplasms, the hope is that paraneoplastic syndromes will become less important as clinical problems.

F. ANTHONY GRECO, MD
Professor of Medicine
Director, Medical Oncology
Vanderbilt University School of Medicine
Nashville, Tennessee

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'The Care and Well-being of Patients'

WHEN ONE THINKS about it, it is surprising that the formally stated purposes of most medical associations make no mention of the care and well-being of patients. This has been true of the California Medical Association, it is true of the American Medical Association and we suspect it is true of most of the associations that comprise what we know as organized medicine. No doubt the care and well-being of patients has always been taken for granted by those within and without the profession. But this may no longer always be the case. It has come to pass that there are those who believe that medical associations are first and foremost physicians' protective associations.

And so if someone, perhaps a young newspaper reporter about to write a story, were to go to a public library and look up the stated purposes of a medical association, what would he or she find? In the case of the California Medical Association, the purposes until recently were "to promote the science and art of medicine, the protection of the public health, and the betterment of the medical profession." There was not a word about patients or patient care, which is what many in the profession believe we are all about.

Upon recommendation of a committee on long-range planning, the 1986 House of Delegates of the California Medical Association changed the purposes in the association's constitution to read "to promote the science and art of medicine, *the care and well-being of patients,* the protection of the public health, and the betterment of the medical profession."

In this writer's view, the newly worded statement not only gives public expression to a purpose that has been there all the time, but also places the series of organizational commitments in the proper sequence of their relative importance. We hope that other organizations within organized medicine will soon place "the care and well-being of patients" high on their masthead for all to see, and in doing so legitimatize organizationally the role of patient advocacy now being espoused by the leadership of our profession.

MSMW

Typhoid Fever—'Recherches du Temps Perdu'

FROM TIME TO TIME we see on our wards a patient with a classic disease, one which reminds us of times past in our own medical history. In the case of typhoid fever, the disease not

only has a dramatic past but remains an important issue in many developing countries.

Typhoid fever has had a significant place in the history of American medicine. The initial inspiration came from Pierre-Charles-Alexandre Louis, Professor of Medicine in Paris during the 19th century, who wrote the classic description of the disease, attaching to it the name "typhoid" *(fievre typhoide),* which refers to the cloudy or stuporous state so often seen in its victims. Among the many American physicians studying under Louis was William Wood Gerhard of Philadelphia, who later differentiated typhoid fever from typhus. Other influential students of Louis who returned to America to carry the lessons of typhoid fever were James Jackson, Jr, and George C. Shattuck of Boston and Alfred Stillé of Philadelphia.

The importance of typhoid fever in America was recognized by Elisha Bartlett who devoted the first chapter to this subject in his landmark book, *The History, Diagnosis, and Treatment of the Fevers of the United States,* published in 1842. Typhoid fever wrought havoc in Colonial America and it proved to be a devastating disease in our Civil War and in the training camps of the Spanish-American War.

Sir William Osler believed that the medical students could learn all of the important lessons of their art by caring for a patient with typhoid fever. The first chapter of his textbook, *The Principles and Practices of Medicine,* published in 1892, was devoted to this disease. His clinical descriptions, based on 1,889 cases in patients at the Montreal General Hospital over a 20-year period, are illuminating, vivid and highly personal. Indeed, many features of the patient's illness described in the Clinicopathologic Conference in this issue are to be found in Osler's textbook, which became the vade mecum of medicine for several generations of American students. Reading the pages of his textbook today, one can almost imagine Sir William on his famous bedside rounds discoursing on this unfortunate young man with a hectic, multisystem illness that brought him to the brink of disaster.

The diagnosis of typhoid fever remains pretty much the same now as it was in Osler's day: by isolating the organism from the bloodstream or feces. Treatment has certainly improved since that era, the most dramatic advance occurring nearly 40 years ago with the introduction of chloramphenicol. In my view, and in the view of others,[1] there is not much reason to believe that any of the more recent antimicrobial drugs have improved on this original antibiotic treatment.

Mortality rates of typhoid fever have fallen dramatically, as shown in Table 4 of the Conference, which reports only one death in 126 typhoid patients seen in recent years at the Los Angeles County-University of Southern California Medical Center. Yet, depressingly high mortality rates are still seen in developing countries, reminding us that modern antibiotics cannot overcome the problems of malnutrition and delayed treatment in typhoid fever.

Osler recognized the importance of nutrition and supportive therapy. Although he notes in his textbook mortality rates from 10% to 30%, his own experience in Montreal was a mortality rate of 11%, which diminished to between 5% and 6% when strenuous efforts were taken to lower fever.

The recommended approach to combating high fever was "hydrotherapy"—that is, immersion in tepid baths when the fever excelled 39.2°C (102.5°F). In one of his letters to his house physicians, Osler describes the treatment of typhoid fever in Freiburg, Germany, in 1890. Their vigorous approach to reducing fever by hydrotherapy led to a mortality rate of 8%. He also noted that they did not use "internal antipyretics." Reduction of fever and maintenance of nutrition were the mainstays of therapy for typhoid fever until the mid-20th century, when chloramphenicol was introduced.

Although not an exact counterpart of Osler's antipyretic approach, a short course of corticosteroids is being used by many experienced clinicians in the modern era to treat severe, life-threatening typhoid fever. In my own experience in the tropics and occasionally with severe cases in the United States, this therapy can have a remarkable effect on alleviating the toxicity and delirium of the more severe forms of this disease. The widespread and mostly underground use of steroids in this manner no doubt prompted the interesting comparative study published by Hoffman and co-workers in which they showed a significant reduction in mortality among steroid-treated patients with severe typhoid fever, compared with placebo-treated controls.[2] As other observers have noted in their own practice, there were no steroid-induced complications in this series.

Antimicrobial treatment has certainly reduced mortality, as well as one of the feared complications seen in the case described in this issue, that of gastrointestinal hemorrhage. Interestingly, antimicrobial treatment has not changed the incidence of intestinal perforation, usually occurring in Peyer's patches in the ileum, nor the occurrences of relapses and chronic carriers. We have learned, however, to be more aggressive in direct surgical intervention of intestinal perforation, and early operative intervention has no doubt saved many lives that would have been lost with the traditional watch-and-wait approach.[3,4]

Typhoid fever continues to be a major health problem in many developing countries. Despite antibiotics, steroids and surgery, the disease is awesome, particularly in a malnourished patient who has access to only rudimentary health care. For this reason, the encouraging news of an effective oral vaccine is particularly welcome.[5]

While modern textbooks of medicine relegate typhoid fever to the back pages, it is still headline news in many parts of the world. For the young man described herein, typhoid fever was a "first-chapter" event, and it is fortunate for him that his doctors remembered the lessons of times past.

SHERWOOD L. GORBACH, MD
Infectious Disease Division
New England Medical Center Hospitals
Boston

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